

Development of Hematopoietic Stem Cell-Engineered Invariant Natural Killer T Cell Therapy for Cancer.

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Public Summary:

Invariant natural killer T (iNKT) cells are potent immune cells for targeting cancer; however, their clinical application has been hindered by their low numbers in cancer patients. Here, we developed a proof-of-concept for hematopoietic stem cell-engineered iNKT (HSC-iNKT) cell therapy with the potential to provide therapeutic levels of iNKT cells for a patient's lifetime. Using a human HSC engrafted mouse model and a human iNKT TCR gene engineering approach, we demonstrated the efficient and long-term generation of HSC-iNKT cells in vivo. These HSC-iNKT cells closely resembled endogenous human iNKT cells, could deploy multiple mechanisms to attack tumor cells, and effectively suppressed tumor growth in vivo in multiple human tumor xenograft mouse models. Preclinical safety studies showed no toxicity or tumorigenicity of the HSC-iNKT cell therapy. Collectively, these results demonstrated the feasibility, safety, and cancer therapy potential of the proposed HSC-iNKT cell therapy and laid a foundation for future clinical development.

Scientific Abstract:

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